Blue Cross Blue Shield Blue Care Network of Michigan

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Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

RETIRED

Effective Date: 12/09/2021

Pepaxto® (melphalan flufenamide)

FDA approval: February 26, 2021
HCPCS: J9999, C9080
Benefit: Medical

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved indication
   b. FDA approved age
   c. Patient must have been treated with four prior therapies including all of the following:
      i. An anti-CD38 monoclonal antibody
      ii. A proteasome inhibitor
      iii. An immunomodulatory agent
   d. The patient has measurable disease with at least one of the following:
      i. Serum M-protein ≥ 0.5 g/dL
      ii. Urine M-protein ≥ 200 mg/24 hours
      iii. Involved serum free light chain assay ≥ 10 mg/dL
      iv. An abnormal serum free light chain ratio of less than 0.26 or greater than 1.65
   e. Use in combination with dexamethasone
   f. ECOG performance status of 0 - 2
   g. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in BCBSM/BCN's utilization management medical drug list.

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing
   b. Authorization Period: 6 months at a time
   c. Renewal Criteria: Treatment may be continued until disease progression or until unacceptable toxicity occurs

***Note: Coverage may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Therapeutic considerations:

A. **FDA approved indication / Diagnosis**

**Please refer to most recent prescribing information.*

B. **Background Information**

a. Pepaxto is an alkylating drug indicated in combination with dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and one CD38-directed monoclonal antibody. Pepaxto is not indicated and is not recommended for use as a conditioning regimen for transplant outside of controlled clinical trials.

b. Safety and efficacy were evaluated in the HORIZON study, a single arm, open-label, phase II study of 157 patients with relapsed or refractory multiple myeloma, of whom 97 were triple-class refractory and had received at least four prior lines of treatment. Patients were refractory to at least one proteasome inhibitor, at least one immunomodulatory agent, and a CD38-directed monoclonal antibody. Patients were included in the study if they had measureable disease defined as serum M-protein greater than or equal to 0.5 g/dL, urine M-protein greater than or equal to 200 mg/24 hours, involved serum free light chain assay greater than or equal to 10 mg/dL, or an abnormal serum free light chain ratio of less than 0.26 or greater than 1.65. Patients were excluded from the trial if they had an ECOG score greater than 2. Patients were given 40 mg Pepaxto every 4 weeks in combination with 40 mg dexamethasone weekly until disease progression or unacceptable toxicity. The primary endpoint was overall response rate which was 23.7% with a median duration of response (DoR) of 4.3 months.

c. Pepaxto has only been studied in combination with dexamethasone and therefore, should only be used in combination with dexamethasone for the treatment of multiple myeloma.

C. **Efficacy**

**Please refer to most recent prescribing information.*

D. **Medication Safety Considerations**

**Please refer to most recent prescribing information.*

E. **Dosing and administration**

**Please refer to most recent prescribing information.*

F. **How supplied**

**Please refer to most recent prescribing information.*

References:

1. Pepaxto [prescribing information]. Waltham, MA: Oncopeptides Inc.; February 2021.
2. National Comprehensive Cancer Network. Multiple myeloma (Version 4.2021). 2020 Dec 10. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed on March 1, 2021.
3. Richardson PG, Oriol A, Larocca A, et al. Melflufen and dexamethasone in heavily pretreated relapsed and refractory multiple myeloma. J Clin Oncol. 2021 Mar 1; 39 (7): 757 – 67.

<table>
<tr><th colspan="3">Policy History</th></tr>
<tr><th>#</th><th>Date</th><th>Change Description</th></tr>
<tr><td>1.3</td><td>Effective Date: 12/09/2021</td><td>Retiring policy as product has been removed from the market</td></tr>
<tr><td>1.2</td><td>Effective Date: 05/24/2021</td><td>PA added to BCNA, MAPPO, BCN, and BCBS
<table><tr><th>Line of Business</th><th>PA Required (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>Yes</td></tr><tr><td>BCNA</td><td>Yes</td></tr></table></td></tr>
<tr><td>1.1</td><td>Effective Date: 04/08/2021</td><td>New Policy</td></tr>
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** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*